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Photochemistry

Stable Meisenheimer Complexes as Powerful Photoreductants Readily Obtained from Aza-Hetero Aromatic Compounds

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Abstract: Excited states of radical anions derived from the photoreduction of stable organic molecules are suggested to serve as potent reductants. However, excited states of these species are too short-lived to allow bimolecular quenching processes. Recently, the singlet excited state of Meisenheimer complexes, which possess a long-lived excited state, was identified as the competent species for the reduction of challenging organic substrates (−2.63 V vs. SCE, saturated calomel electrode). To produce reasonably stable and simply accessible different Meisenheimer complexes, the addition of *n*BuLi to readily available aromatic heterocycles was investigated, and the photoreactivity of the generated species was studied. In this paper, we present the straightforward preparation of a family of powerful photoreductants ($^*E_{ox} < -3$ V vs. SCE in their excited states, determined by DFT and time-dependent TD-DFT calculations; DFT, density functional theory) that can induce dehalogenation of electron-rich aryl chlorides and to form C–C bond through radical cyclization. Photophysical analyses and computational studies in combination with experimental mechanistic investigations demonstrate the ability of the adduct to act as a strong electron donor under visible light irradiation.

Introduction

Electron-rich alkenes with neutral or anionic substituents have been used as strong reducing agents, and those that reduce aryl halides to aryl radicals or aryl anions are routinely called super electron donors.[1] These compounds were introduced as an alternative to metal-based reducing reagents.[2] A guiding idea for the preparation of super-reductants involves the installation of strong electron donor groups (EDG) surrounding an alkene moiety, for example in tetrakis(dimethylamino)ethene, TDAE.[3] The single electron transfer (SET) chemistry of electron-rich alkenes has been intensively studied in recent years.[4] This class of molecules reduces an array of functional groups, such as iodoarenes, alkyl halides, arenesulfonamides, triflates, triflamides, Weinreb amides, and acyloin derivatives, and can replace heterogeneous reductants, such as Zn^0 or Mn^0, in homogeneous Ni-catalyzed cross-electrophile coupling reactions.[5] Investigations on organic photoreductants were mainly carried out by Murphy,[6] and their reactivity was also analyzed by theoretical models.[7] Remarkably, under photoactivation with visible light an even more reducing behavior was observed (Figure 1),[8] unlocking the hydrodehalogenation of electron-rich halo-arenes,[9] such as chloro anisole derivatives. TDAE was found by Wenger to be the strongest reductant under light irradiation, able to reduce aryl chlorides (Figure 1).[10] Light can increase chemical redox potential, via photoinduced electron transfer (PET), and new applications of photochemistry have attracted great attention over the last decades.[11]

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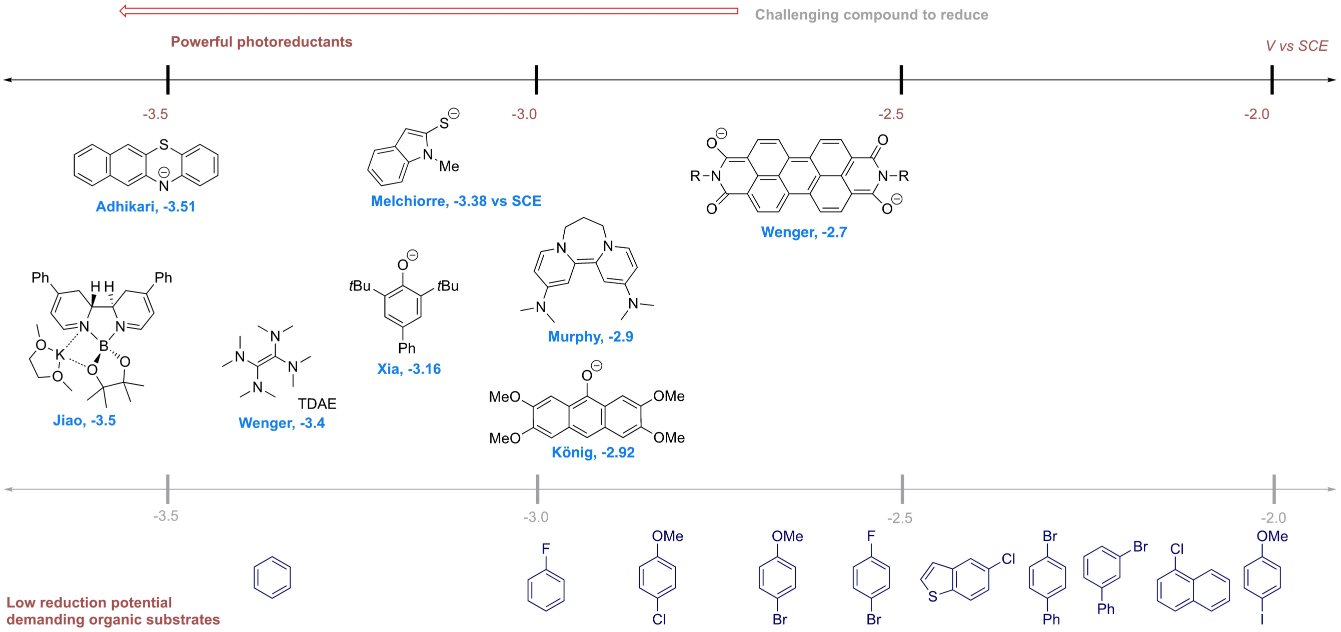

Challenging compound to reduce
Powerful photoreductants
V vs SCE
-3.5
-3.0
-2.5
-2.0
Adhikari, -3.51
Melchiorre, -3.38 vs SCE
Wenger, -2.7
Jiao, -3.5
Wenger, -3.4
TDAE
Xia, -3.16
Murphy, -2.9
König, -2.92
Low reduction potential demanding organic substrates

Figure 1. Reduction potentials of various powerful photocatalysts, stoichiometric and catalytic photoreductants, and aryl halides.

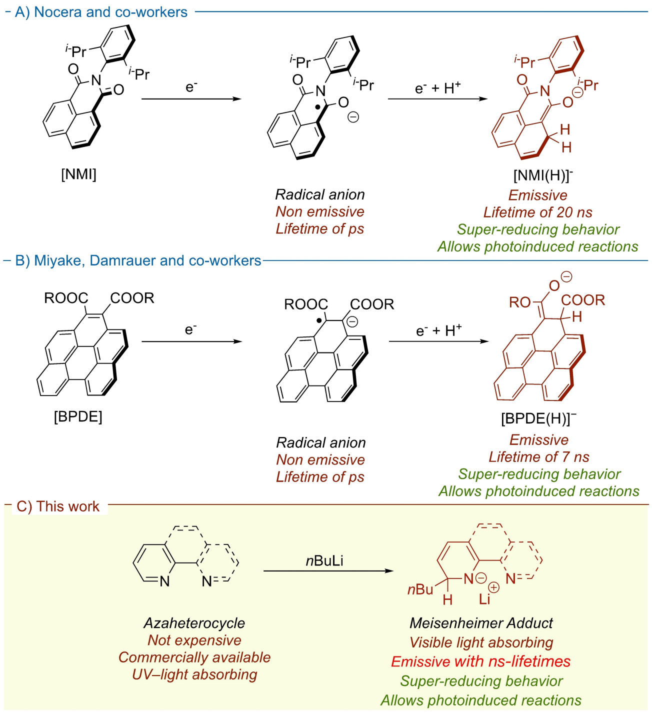

A) Nocera and co-workers
[NMI]
e⁻
Radical anion
Non emissive
Lifetime of ps
e⁻ + H⁺
[NMI(H)]⁻
Emissive
Lifetime of 20 ns
Super-reducing behavior
Allows photoinduced reactions
B) Miyake, Damrauer and co-workers
[BPDE]
e⁻
Radical anion
Non emissive
Lifetime of ps
e⁻ + H⁺
[BPDE(H)]⁻
Emissive
Lifetime of 7 ns
Super-reducing behavior
Allows photoinduced reactions
C) This work
Azaheterocycle
Not expensive
Commercially available
UV–light absorbing
nBuLi
Meisenheimer Adduct
Visible light absorbing
Emissive with ns-lifetimes
Super-reducing behavior
Allows photoinduced reactions

Figure 2. Meisenheimer complexes as described by A) Nocera, B) Miyake and Damrauer, and C) our concept.

Examples of highly reducing photocatalysts obtained from electron-rich closed-shell anions,[12] capable of reducing arylchlorides, are summarized in Figure 1.[13] Anionic electron-rich compounds are also accessible by forming relatively stable reactive intermediates. Highly colored Meisenheimer complexes have a long history and a rich chemistry.[14,15] Quite recently, Nocera described a Meisenheimer adduct (namely, $[NMI(H)]^-$ $[TBA]^+$ (TBA = tetrabutylammonium, Figure 2A) deriving from the two-electron reduction and protonation of naphthalene monoamide (NMI).[16]

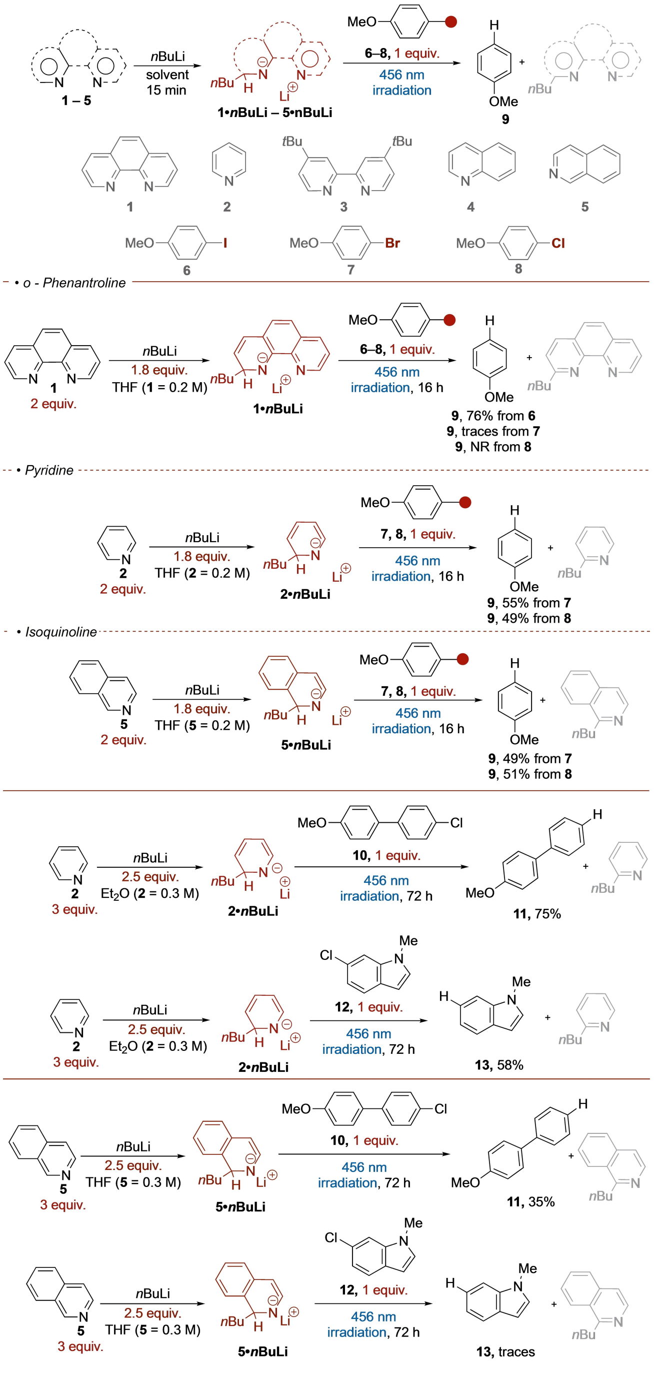
The singlet excited state of $[NMI(H)]^-$ is a potent reductant at −2.7 V vs. SCE, (SCE, saturated calomel electrode). It is long-lived (20 ns), and its emission was dynamically quenched with chloroarene under 440 nm irradiation. Miyake and Damrauer, in a recent paper,[17] employed BPDE (benzo[ghi]perylene diester, Figure 2B) to generate the Meisenheimer adduct $[BPDE(H)]^-$, a two-electron, one-proton activated closed-shell super-reductant, capable to promote the direct reduction of inert substrates like benzene and fluorobenzene. Besides these two examples of Meisenheimer adducts that are obtained under peculiar conditions, other nucleophiles and aromatic substrates may produce similarly photoactive Meisenheimer adducts, for the efficient, and reproducible photo reduction of challenging C–X bonds.[18] The stability and relatively easy preparation of adducts derived from the addition of alkyllithium[19] or Grignard reagents[20] to azaheterocycles[21] (pyridine, quinoline, isoquinoline, phenanthroline, etc.) attracted our interest. The addition of organometallic reagents to phenanthroline and successive oxidation by air or MnO_2 is a well-established methodology,[22] first proposed by Sauvage,[23] to prepare tailored phenanthroline derivatives. Besides phenanthroline derivatives,[24] other π-poor aromatic heterocycles, such as pyridines,[25] are susceptible to nucleophilic addition of organometallic reagents or hydrides.[26] The well-known 1,2 nucleophilic addition of alkylithium reagents to pyridine was recently reinvestigated by Mulvey,[27] and his new approach allowed to isolate and characterize Meisenheimer adducts, such as lithium hydride surrogate complexes[28] that can perform interesting catalytic reactions.[29]

Herein, we report a comprehensive investigation of the use of commercially available heterocyclic compounds for the in situ preparation of stable Meisenheimer adducts (Figure 2C).[30] Their behavior as super-reductants under visible light irradiation was examined in benchmark reductions of electron-rich arenes (Ar–X, X = I, Br, Cl). The adduct of pyridine or isoquinoline with *n*BuLi resulted in the best photoreductans which were applied in the reduction of several haloaromatic compounds. The aryl radical generated under the reaction conditions also triggered radical cyclizations, effectively incorporating the aryl moiety in cyclic structures. The Meisenheimer adducts of quinoline and isoquinoline were isolated and investigated through photophysical analysis and computational studies, to shed light on their behavior, and illustrate the potential of our methodology.

Results and Discussion

We started to examine simple Meisenheimer adducts obtained by the addition of *n*BuLi at 0 °C to commercially available heterocyclic compounds. To assess their photoreductive capabilities under light irradiation, we initially selected phenanthroline **1**, pyridine **2**, 4,4′-di-*tert*-butyl-2,2′-dipyridyl **3**, quinoline **4**, and isoquinoline **5** as starting materials.[31]

The corresponding Meisenheimer adducts were obtained by the direct addition of a slight *n*BuLi defect at 0 °C inside a Young® flask containing the heteroaromatic compound and the solvent. For all the selected heterocycles, the addition of *n*BuLi caused the colorless solutions to turn yellow.[32] To test the reduction ability of our Meisenheimer adducts, we selected the stoichiometric photochemical hydrodehalogenation of aryl halides as benchmark reactions. Specifically, we used 4-iodoanisole (**6**, $E_{red} = -2.0$ vs. SCE), 4-bromoanisole (**7**, $E_{red} = -2.5$ vs. SCE), and 4-chloroanisole (**8**, $E_{red} = -2.9$ vs. SCE) to assess their reductive power and identify the most efficient reductants for further studies (Scheme 1). After 15–30 min. the aryl halide **6**, **7**, or **8** was added to the in situ generated photoactive species, and the reaction mixture was irradiated (456 nm, Kessil lamp, 40 W) for 16 hours, and the outcome of the reaction was analyzed by HPLC. The data show that the reducing ability of the Meisenheimer adduct is strongly influenced by the nature of the heterocycles. The phenanthroline Meisenheimer adduct was able to reduce 4-iodoanisole, but not the 4-chloro or 4-bromo anisole (for the full study and evaluation of the conversions regarding hydrohalogenation with other heterocyclic compounds, see Table S1). Among the different heterocycles, pyridine and isoquinoline displayed the strongest reduction ability and the corresponding Meisenheimer adducts have proven capable of promoting, under visible light irradiation, the reduction of 4-chloroanisole in satisfactory yields. In all cases, we observed the formation of the alkylated heterocyclic compounds, that, in some experiments, were isolated in quantitative yields by chromatography. Notably, through GC-MS analysis, the identification of radical-radical coupling products between the alkylated heterocycle and the dehalogenated aryl halide was observed. The amount of byproduct (ranging from 5 % to 20 %) depended on the nature of the heterocycle and the reaction conditions.


1 – 5
nBuLi
solvent
15 min
1•nBuLi – 5•nBuLi
6–8, 1 equiv.
456 nm
irradiation
MeO
OMe
9
nBu
tBu
1
2
3
4
5
6
7
8
I
Br
Cl
• o - Phenantroline
1
2 equiv.
nBuLi
1.8 equiv.
THF (1 = 0.2 M)
1•nBuLi
6–8, 1 equiv.
456 nm
irradiation, 16 h
9, 76% from 6
9, traces from 7
9, NR from 8
• Pyridine
2
2 equiv.
nBuLi
1.8 equiv.
THF (2 = 0.2 M)
2•nBuLi
7, 8, 1 equiv.
456 nm
irradiation, 16 h
9, 55% from 7
9, 49% from 8
• Isoquinoline
5
2 equiv.
nBuLi
1.8 equiv.
THF (5 = 0.2 M)
5•nBuLi
7, 8, 1 equiv.
456 nm
irradiation, 16 h
9, 49% from 7
9, 51% from 8
2
3 equiv.
nBuLi
2.5 equiv.
Et2O (2 = 0.3 M)
2•nBuLi
10, 1 equiv.
456 nm
irradiation, 72 h
11, 75%
12, 1 equiv.
Me
13, 58%
5
3 equiv.
nBuLi
2.5 equiv.
THF (5 = 0.3 M)
5•nBuLi
10, 1 equiv.
11, 35%
12, 1 equiv.
13, traces

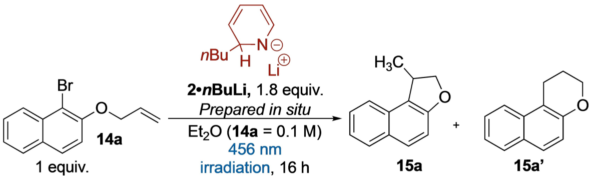
Scheme 1. Photoinduced hydrohalogenation of halo aromatic compounds in the presence of different Meisenheimer adducts.

To further substantiate the results, two electron-rich non-volatile aryl chlorides were tested under the above reductive conditions. Namely, 4-chloro-(4′-methoxybiphenyl) **10** and 6-chloro-1-methyl-1H-indole **12** were tested both in the presence of **2·*n*BuLi** and **5·*n*BuLi**. In the case of **2·*n*BuLi**, the reaction was performed in Et_2O considering the results obtained for the intramolecular radical cyclization (see below). While the excited state of **2·*n*BuLi** proved to be an effective reductant for **10** and **12**, **5·*n*BuLi** provided modest results only in the reduction of **10**. The superior reducing power of Meisenheimer adducts obtained from isoquinoline and pyridine was evident, and these heterocyclic compounds were selected for further studies.

The versatile chain process of radical cyclization of aryl halides is a crucial methodology in organic synthesis and has been widely demonstrated through various applications,[33] including under photoredox conditions.[34] Therefore, we turned our attention to a reductive radical cyclization of challenging substrates. We selected compound **14a** as the model substrate and, as depicted in Table 1, evaluated all the reaction parameters to maximize the reaction outcome.

The Meisenheimer adducts were prepared in situ as described above and the solution was irradiated for 16 h. Pyridine (**2**) served as the precursor of the photoreductant in diethyl ether solution resulting in the synthesis of the desired 1,2-dihydronaphtho[2,1-b]furan derivative **15a** in excellent yields and regioselectivity (>95 %, **15a**:**15a**′ 13:1, Table 1, entry 1). It is important to note that light, *n*BuLi, and pyridine are all essential components for the successful completion of this reaction (Table 1, entries 2,3, and 4 respectively). THF led to enhanced regioselectivity (**15a**:**15a**′ >20:1, Table 1, entry 1) albeit a slight reduction in the overall yield. Phenanthroline (**1·nBuLi**) yielded inferior outcomes in both yield and regioselectivity compared to other reagents (Table 1, entry 7). Using isoquinoline, **5·nBuLi** adducts demonstrated efficacy in THF solution (Table 1, entry 7), yielding results comparable to those achieved using pyridine under similar conditions. Increasing the quantity of Meisenheimer adduct did not result in a proportional increase in reaction yield (refer to Table 1, entry 9). Dioxane and methyl *tert*-butyl ether (MTBE) were found unsuitable as solvents for the reaction, as no product was observed after the irradiation (Table 1, entries 10 and 11). The addition of a hydrogen atom transfer (HAT) donor like 1,4-cyclohexadiene improved the isolated yields but was not crucial (Table 1, entry 12). With the optimized reaction conditions in hand, the scope of the photo-promoted reductive cyclization was evaluated for a broad set of substituted aryl halides (Scheme 2). 1,2-Dihydronaphtho[2,1-*b*]furan derivative **15a** was isolated in excellent yields and regioselectivity (>95 % **15a**:**15a’** 20:1) starting from substrates **14a** and **16a**. The amount of the 6-*endo* adducts increased (**15a**:**15a’** 5:1) with the chloro derivative **17a**. However, yields were moderate (55 %) under slightly modified reaction conditions. In the survey of substrates, the nature of the olefin acceptor moiety was modified, and the radical reaction was tested. The cyclization results were quite selective and the results were comparable with reported procedures.[33,34] The presence of the 6-*endo* products was detected only in minor amounts.[35]

Table 1: Optimization of the reaction conditions for photoinduced radical cyclization in the presence of Meisenheimer adducts.



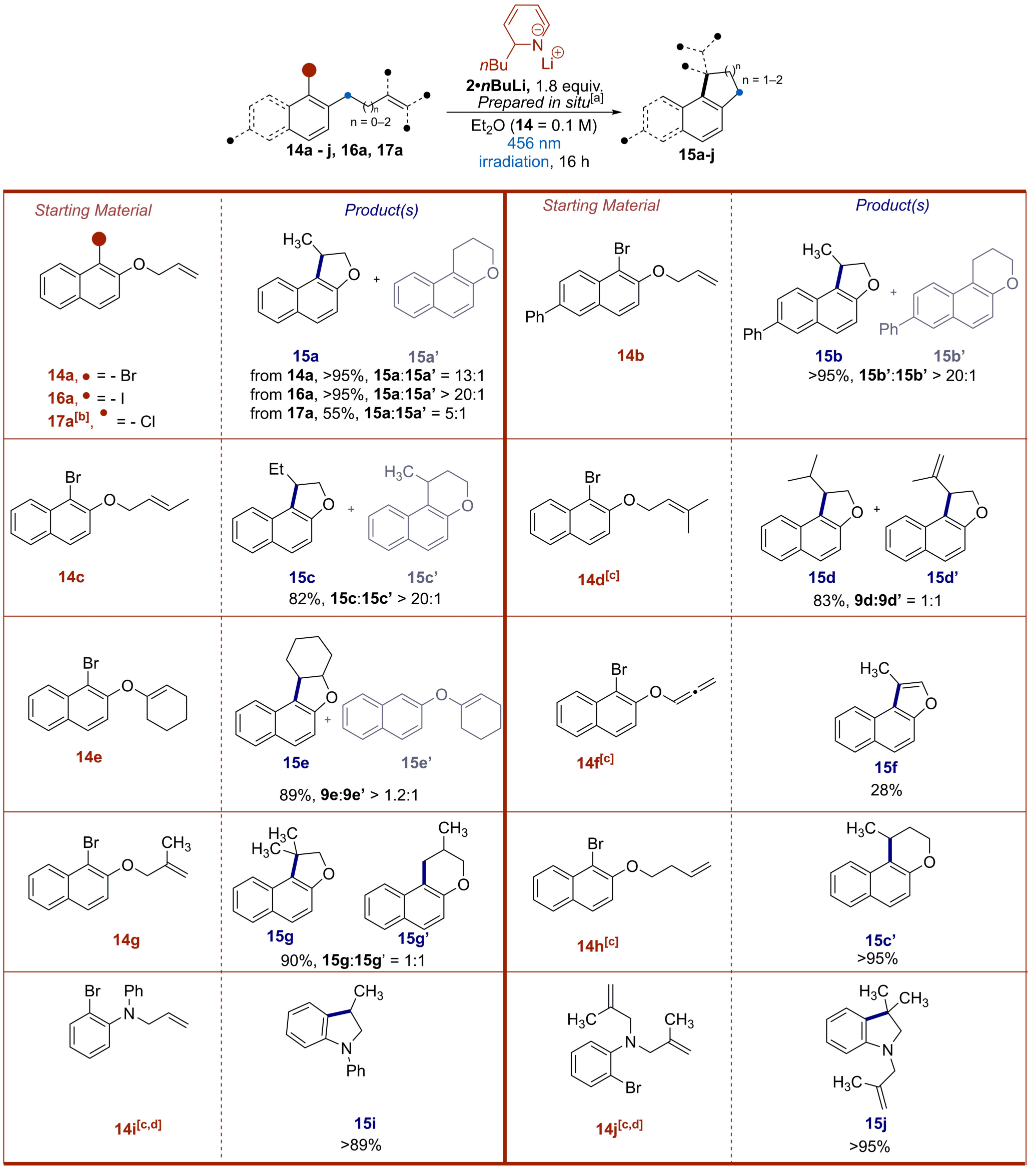
Entry[a]	Deviation from standard conditions	Yield (%)[b]	15a:15a′[c]
1	None	>95	13:1
2	No light	NR	–
3	No *n*BuLi	NR	–
4	No **2**	NR	–
5	5 h irradiation time	93	10:1
6	THF instead of Et_2O	62	>20:1
7	**1·*n*BuLi** instead of **2·*n*BuLi**[d]	16	8:1
8	**5·*n*BuLi** instead of **2·*n*BuLi**[d]	71	9:1
9	**5·*n*BuLi** instead of **2·*n*BuLi**[d,e]	61	9:1
10	**5·*n*BuLi** instead of **2·*n*BuLi**[f]	NR	–
11	**5·*n*BuLi** instead of **2·*n*BuLi**[g]	NR	–
12	**5·*n*BuLi** instead of **2·*n*BuLi**[d,h]	75	6:1

[a] Reaction performed on 0.15 mmol scale of **14a**. [b] Isolated yield after chromatographic purification. [c] Evaluated by ^1H NMR analysis of the reaction crude. [d] Reaction performed in THF. [e] **5·*n*BuLi** 4.4 equiv. (Prepared from 5 equiv. of **5** and 4.4 equiv. of *n*BuLi). [f] Reaction performed in dioxane. [g] Reaction performed in MTBE (methyl *tert*-butyl ether) [h] 1.1 equiv. of 1,4-cyclohexadiene added. NR = no reaction.

Cyclization involving primary or secondary alkyl radical intermediates proceeded in good yields. The formation of the six-membered rings, enabled by the 6-*exo-trig* cyclization was possible, as demonstrated for **14h**. We have also employed substrate **14e** with a cyclic vinyl ether. For this substrate, the cyclization reaction is difficult, and the cyclized product was isolated together with the dehalogenated starting material. Remarkably, the decoration of the naphthol moiety with a metallyl pendant (**14d)** gave two products in a 1:1 ratio (**15d** and **15d**′). In this scenario, the quenching of the tertiary radical through a HAT step required for the formation of the desired product (**15d**), competes with the elimination of the H• leading to the formation of the C=C double bond. To further expand the substrate‘s scope for this reaction, we have briefly examined the cyclization of allylic aromatic amines, adding one or two allylic chains to the nitrogen. Also in these cases, the reaction was better promoted by **2·*n*BuLi**. In most cases, desired products were obtained in high or quantitative yields, and it was possible to isolate the pure product after an acidic workup (three extractions with 2 M HCl) without the need for chromatography. Finally, the employment of allenylic substrate was attempted, and the aromatic furan derivative **15f** was isolated in modest yields.

To further expand the chemical reactivity space of our photoactive Meisenheimer adducts, we moved our attention to other challenging reductive transformations.

Sulfonamides are useful amine protecting groups thanks to their inertia to acids, bases, electrophiles, and stability under oxidizing and mild reduction conditions.[36] However, the main drawback in the use of this protecting group is related to its difficult cleavage, often requiring harsh


nBu
Li
N
n = 0–2
14a - j, 16a, 17a
2•nBuLi, 1.8 equiv.
Prepared in situ[a]
Et2O (14 = 0.1 M)
456 nm
irradiation, 16 h
n = 1–2
15a-j
Starting Material
Product(s)
Starting Material
Product(s)
14a, ● = - Br
16a, ● = - I
17a[b], ● = - Cl
15a
15a'
from 14a, >95%, 15a:15a' = 13:1
from 16a, >95%, 15a:15a' > 20:1
from 17a, 55%, 15a:15a' = 5:1
14b
15b
15b'
>95%, 15b':15b' > 20:1
14c
15c
15c'
82%, 15c:15c' > 20:1
14d[c]
15d
15d'
83%, 9d:9d' = 1:1
14e
15e
15e'
89%, 9e:9e' > 1.2:1
14f[c]
15f
28%
14g
15g
15g'
90%, 15g:15g' = 1:1
14h[c]
15c'
>95%
14i[c,d]
15i
>89%
14j[c,d]
15j
>95%

Scheme 2. Scope evaluation for photoinduced Intramolecular radical cyclization. [a] Meisenheimer adduct was prepared in situ combining 2 equiv. of azaheterocycle and 1.8 equiv. of *n*BuLi. [b] 50 h irradiation time. [c] Deviation from model reaction conditions: 2.5 equiv. of **2·nBuLi** employed for the reaction. Meisenheimer adduct was prepared in situ combining 3 equiv. of azaheterocycle and 2.5 equiv. of *n*BuLi. [d] Product isolated without chromatographic purification. Acidic work-up (2 M HCl) revealed sufficient for purification.

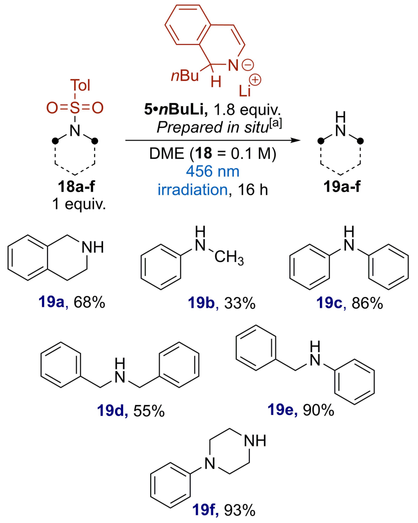
reaction conditions.[37] Electrochemical or strongly reducing agents such as SmI_2 are often employed.[38] Photoredox methodologies, with the possibility to create strongly reducing conditions, recently opened new ways for the removal of this group, leading to the unprotected amine.[39] Scheme 3 illustrates the reactions of our strong photoreductants with tosyl amines. The reaction is promoted in DME using 1.8 equiv. of the isoquinoline adduct **5·*n*BuLi** (for the reaction optimization, see Table S2, SI).

The reaction yielded moderate to high yields and proved to be highly substrate-dependent, with dialkyl amides giving better yields. However, the strong basicity/nucleophilicity of the Meisenheimer adducts limits the class of compounds in which the cleavage is applicable, but the presence of functional groups was not investigated in detail.

After exploring the synthetic potential of these new powerful reactants, we sought to fully elucidate the mechanism of the reaction and the parameters that control the reactivity of lithiated azaheterocyclic compounds, we undertook photophysical and computational studies in combination with experimental mechanistic evidence.

Photophysical Study

Compound **5·*n*BuLi** (prepared according to the procedure described in the SI) was analyzed employing steady-state



Scheme 3. Scope evaluation for photoinduced detosylation of amines. [a] Meisenheimer adduct was prepared in situ combining 2 equiv. of **5** and 1.8 equiv. of *n*BuLi.

absorption and time-resolved luminescence spectroscopy in deaerated THF solution.

At high concentrations (ca. 25 mg/mL) it shows a low-energy absorption band that spans the visible spectrum up to ca. 700 nm, leading to brick red-colored solutions in agreement with literature reports on similar compounds.[40] The absorption bands of **5⋅*n*BuLi** in the visible spectrum are likely attributable to the formation of oligomeric adducts present at higher concentrations in solution. Therefore, the absorption profiles of **5⋅*n*BuLi** are significantly affected by the concentration (see Figure S6–7, SI): for diluted samples (0.1 mg/mL), the lowest energy absorption band shifts to higher energy, so that the adducts are less effective in harvesting visible light ($\lambda > 400$ nm), in analogy to what is observed for organo-alkali metal complexes.[41]

In deaerated THF solutions, compound **5⋅*n*BuLi** (ca. 25 mg/mL) displays excitation-dependent emission bands: a red-shift is observed upon increasing the excitation wavelength (λ_{ex} from 450 to 580 nm, see Figure 3B and Figure S8 for details), indicating the presence of multiple emissive species corresponding to oligomeric complexes with different sizes. Similarly, the corresponding emission lifetimes are dependent on the emission wavelength, with multiexponential decays ranging between 1.1 and 22.9 ns (see Figure S9). Interestingly, longer-lived components become predominant at higher emission wavelengths. Similarly to absorption spectra, changes in the emission bands are observed upon sample dilution (see Figure S10 for **5⋅*n*BuLi**). It is worth noting that the parent molecule **5** does not show any absorption band in the visible spectral region, with its spectrum dominated by π–π* or n–π* electronic transitions in the UV region (up to ca. 320 nm for **5**).[42] Furthermore, the fluorescent excited state decays with a shorter lifetime of 0.25 ns in polar solvents.[43,44]

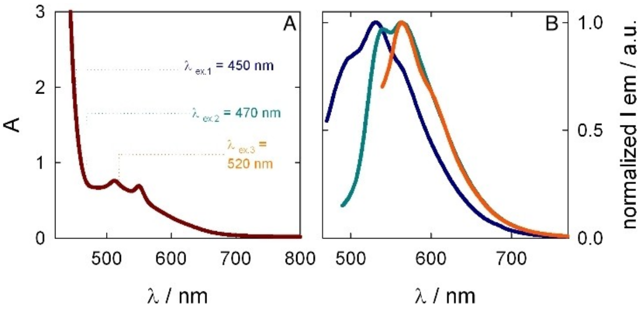


Figure 3. A: absorption spectrum of **5⋅*n*BuLi** in deaerated THF (ca. 25 mg/mL; optical path length: 2 mm). B: normalized emission spectra (front-face configuration) collected from the same sample at selected excitation wavelengths ($\lambda_{ex} = 450$ nm, blue line; $\lambda_{ex} = 470$ nm, green line; $\lambda_{ex} = 520$ nm, orange line).

Computational Characterization

To complement the experimental characterization, we carried out a quantum-chemical investigation on monomeric **4⋅*n*BuLi** and **5⋅*n*BuLi** (in each case including explicitly two THF solvent molecules in the calculations) and then focused on oligomeric complexes of the latter, since clear evidence of aggregation appears from the photophysical study, in line with the known tendency of organolithium compounds to form oligomeric complexes.[45]

The structures we designed as possible aggregates were mostly inspired by previous studies on organolithium aggregates[46] in which several complexes (Figure S20) were proposed. Among these, we selected the dimers and tetramers shown in Figure 4, namely aggregates including an even number of isoquinoline **5** moieties, to maximize the probability of forming aggregates with relevant interactions between pairs of chromophores, that could explain the redshift of absorption and emission spectra observed for higher concentrations. For each selected structure, the **5⋅*n*BuLi** aggregate included in the calculation a variable number of explicit THF solvent molecules, ranging from two to six, that coordinate the lithium atoms. A total of eight

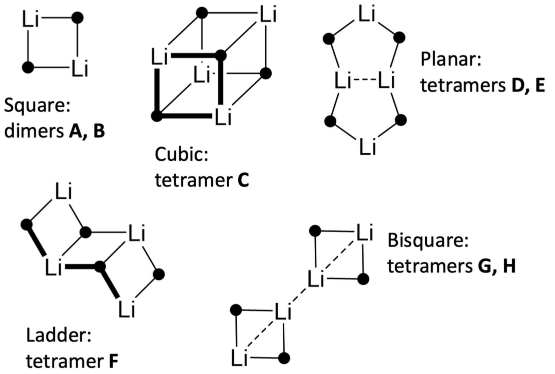


Figure 4. Schematic representation of the **5⋅*n*BuLi** aggregates computationally investigated and label adopted (**A-H**).

aggregate structures (from **A** to **H**, Table S3–5 and Figure 4) were considered.

The predicted absorption spectra of monomeric **4⋅*n*BuLi** and **5⋅*n*BuLi** show, at the lowest excitation energy, an excited state dominated by a local excitation on the quinoline/isoquinoline moiety and, at higher energy, an excitation corresponding to charge transfer (CT) from N to Li. This is also demonstrated by comparing the electrostatic potential maps of the ground, lowest excited, and CT states for monomeric **5⋅*n*BuLi** in Figure S25.

Moving to possible oligomeric structures (Figures 4 and S26–S33) most of the aggregates considered did not show red-shifted electronic excitations that could be assigned to the experimentally observed red-shift of the absorption spectrum at higher concentrations. However, TD-DFT calculations at the optimized ground state geometries of aggregates **F**, **G**, and **H** displayed red-shifted absorption bands (Figure S34). Inspection of the optimized ground state structures of these specific oligomers (Figures S31–S33) shows the presence of pairs of closely interacting isoquinoline moieties. To further characterize such a red-shifted absorption, the lowest singlet excited state of **F** and **G**, as exemplary cases, were further investigated and their relaxed structures were determined (Figure 5 and S35). The predicted, red-shifted emissions of aggregates **G** and **F** are in very good agreement with the shift observed experimentally at high concentrations. This suggests that aggregation to form various oligomeric structures is at the origin of the changes detected for both absorption and emission spectra. Notably, the lowest-lying singlet excited state shows typical features that are usually found in excimer states, as seen in Figure 5 for aggregate **G**.

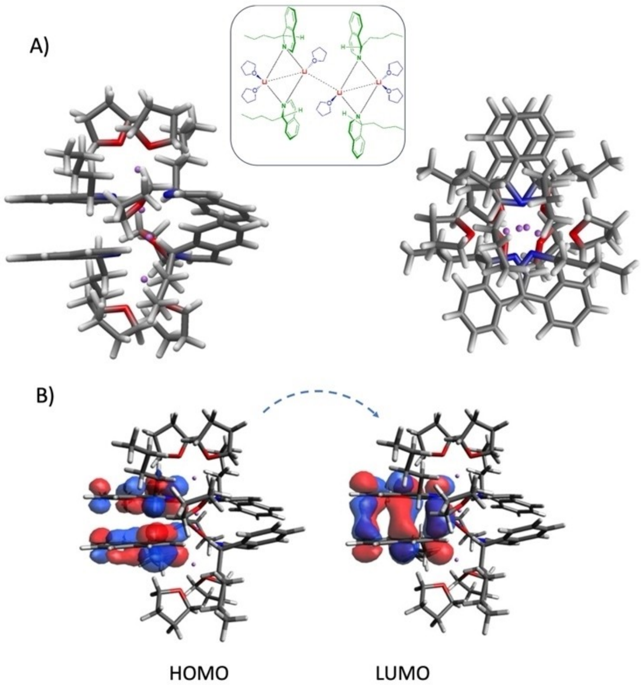


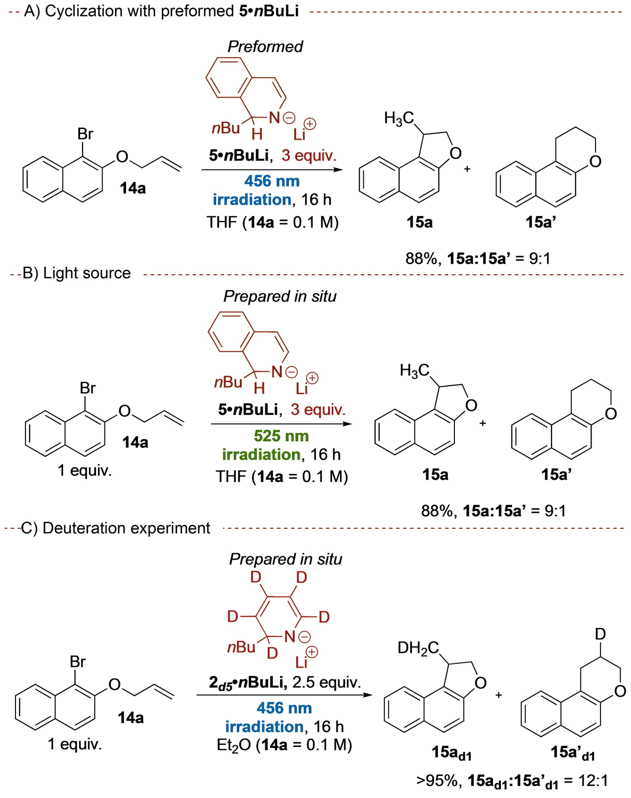
Figure 5. A) Front and side views of the optimized excited state structure of the **5⋅*n*BuLi** aggregate **G** and B) molecular orbitals involved in the excitation (represented by the dashed-line arrow) that characterizes the lowest singlet excited state responsible for red-shifted emission. From TD-ωB97X-D/def2-SVP calculations.

This state is dominated by the electronic HOMO→LUMO excitation where both orbitals are essentially delocalized on a pair of isoquinoline chromophores, with the HOMO displaying an antibonding character and the LUMO a bonding character typical of excimer states. However, in contrast to excimers, in these oligomers the two chromophoric units are held together also in the ground state, driven by aggregation involving the network of lithium ions. As a result, the redshift is not only observed in emission but also absorption. Similar features are found also for **F**, with frontier orbitals delocalized on nearby isoquinoline chromophores (Figure S35).

To conclude, the quantum-chemical investigation on monomeric **5⋅nBuLi** and a selection of oligomeric structures demonstrates that the observed red shift in absorption and emission spectra at high concentrations is due to the formation of oligomeric species. Not all oligomeric species absorb at lower energies, but some of them have been computationally uncovered and display interacting isoquinoline chromophores. In support of the photophysical study, the computational investigation therefore suggests that multiple emissive species may co-exist, characterized by varying absorption and emission spectra. To assess the super-reducing character of the Meisenheimer adducts, we determined the excited state redox potentials of **4⋅*n*BuLi,** **5⋅*n*BuLi** and of the **G** aggregate of **5⋅*n*BuLi**, adopting a direct protocol (See the Supporting Information for discussions and details, Table S6). The oxidation potential of monomeric ***4⋅*n*BuLi** is predicted to be −3.2 eV vs SCE, while monomeric ***5⋅*n*BuLi** and the ***G** oligomeric complex display values in the range of $-3.8 < {}^*E_{ox} < -3.2$ V vs SCE (monomeric structure and aggregate, respectively) supporting the super-reductant character of these adducts.

Mechanistic Studies

Two experiments proved to be instrumental in uncovering the mechanism. Firstly, the isolated **5⋅*n*BuLi** was used in the model radical cyclization (See the Supporting Information for details of the preparation and reaction setup) to demonstrate that the Meisenheimer adduct is the photoactive species that drives the reaction (Scheme 4A). Notably, comparable yields to model conditions were obtained, with product **15a** being successfully isolated. Furthermore, the reaction was also possible upon excitation of the Meisenheimer adduct at 525 nm, as suggested by the absorption spectrum of **5⋅*n*BuLi** (Scheme 4B). Secondly, both the oxidative pathway of the Meisenheimer adduct following the single electron transfer (SET) event and the source of protons required for the formation of the final cyclization product have been demonstrated. By using d_5-pyridine as the precursor of Meisenheimer complex under reaction conditions, it was possible to obtain products **15a**$_{\mathbf{d1}}$ and **15a′**$_{\mathbf{d1}}$ with yields comparable to standard protocols, exhibiting full deuteration on the terminal methylene group


A) Cyclization with preformed 5•nBuLi
Preformed
Br
14a
nBu H N⊖ Li⊕
5•nBuLi, 3 equiv.
456 nm irradiation, 16 h
THF (14a = 0.1 M)
H3C
15a
15a'
88%, 15a:15a' = 9:1
B) Light source
Prepared in situ
1 equiv.
5•nBuLi, 3 equiv.
525 nm irradiation, 16 h
THF (14a = 0.1 M)
88%, 15a:15a' = 9:1
C) Deuteration experiment
Prepared in situ
D D D D nBu D
2d5•nBuLi, 2.5 equiv.
456 nm irradiation, 16 h
Et2O (14a = 0.1 M)
DH2C
15ad1
15a'd1
>95%, 15ad1:15a'd1 = 12:1

Scheme 4. Mechanistic investigation.

of the allyl moiety (Scheme 4C). This result suggests a HAT mechanism for termination of the alkyl radical, upon cyclization which involves the oxidized Meisenheimer adduct.

Combining the photophysical study, the computational modeling, and the experimental evidence a tentative mechanism is depicted in Figure 6. Under visible light irradiation, the in situ-generated Meisenheimer adduct reaches its excited state. The reductive quenching through PET in the presence of the substrates leads to the formation of the aryl radical anion that undergoes fragmentation/dehalogenation and intramolecular reaction with the alkene pendant. The resulting alkyl radical abstracts a hydrogen atom by the oxidized azaheterocycle leading to the rearomatization of the Meisenheimer adduct and the product formation. This mechanistic picture suggests how we have obtained the final products through reduction, cyclization, and H-abstraction reactions. Unfortunately, the rapid HAT-type reaction precludes the possibility of intercepting the radical formed with other species. For example, the use of pyrrole in excess to trap the aryl radical in our reaction was unsuccessful.

Conclusion

We have illustrated how to generate a family of photoactive organic "super-reductants" using accessible, aromatic heterocyclic compounds by employing a simple alkylation reaction with *n*BuLi. The enormous possibility of variation of both heterocycles and organometallic reagents, makes this class of super-reducing agents a vast field of study, both for practical and theoretical applications. Our super-reducing agents reduce substrates with highly negative potential, such as electron-rich aryl chlorides and *N*-tosylamines, and are also capable of inducing radical cyclization reactions. Photophysical and theoretical investigations unveiled the active species formed, and why they behave as super-reductants. Concerning other Meisenheimer adducts capable of acting as super-reductants, the preparation of these species is predictable and straightforward. The presence of stoichiometric sacrificial organic molecules that are always employed in the presence of catalytic "super-reductants" is not necessary. Many interesting subtopics and investigations are now open and are the subject of ongoing studies in our laboratory.

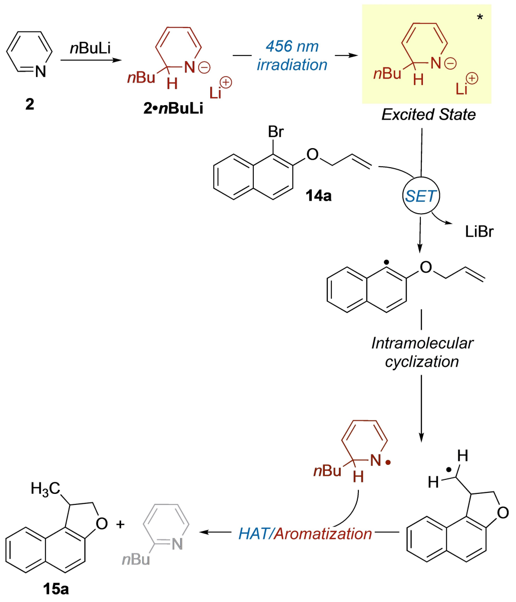

2
nBuLi
2•nBuLi
456 nm irradiation
Excited State
*
Br
14a
SET
LiBr
Intramolecular cyclization
nBu H N•
H
H
HAT/Aromatization
H3C
O
nBu N
15a

Figure 6. Proposed mechanism for photoredox radical cyclization promoted by Meisenheimer adduct.

Supporting Information

The authors have cited additional references within the Supporting Information.[47–78]

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Heterocycles · Meisenheimer adducts · photoredox reactions · superreductant · radical · TDDFT calculations

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[32] The color of the reaction mixture is deeper red for more extended p-systems, suggesting an extensive red shift on the absorption spectrum of the Meisenheimer adduct compared with the neutral heterocycle. On the contrary, when a less conjugated system such as pyridine was used, the solution color was bright yellow suggesting a more modest red shift and a higher energy associated with the excited state. However, aggregation of the lithium derivatives in solution is responsible for the color; see Supporting Information, photophysical and theoretical studies.

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Photochemistry

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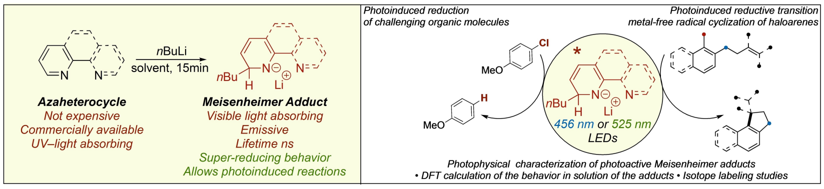
Stable Meisenheimer Complexes as Powerful Photoreductants Readily Obtained from Aza-Hetero Aromatic Compounds


nBuLi
solvent, 15min
N
nBu
H
Li
Azaheterocycle
Not expensive
Commercially available
UV–light absorbing
Meisenheimer Adduct
Visible light absorbing
Emissive
Lifetime ns
Super-reducing behavior
Allows photoinduced reactions
Photoinduced reduction
of challenging organic molecules
Photoinduced reductive transition
metal-free radical cyclization of haloarenes
MeO
Cl
H
456 nm or 525 nm
LEDs
Photophysical characterization of photoactive Meisenheimer adducts
• DFT calculation of the behavior in solution of the adducts • Isotope labeling studies

Strong reducing systems (≤3.0 V vs SCE) can be obtained simply and practically by adding *n*BuLi to available heterocyclic compounds (pyridine, isoquinoline, etc) and using them under irradiation at 456 nm. Strong photoreductans obtained are capable of reducing electron-rich arylchlorides.